REMARKS

Claims 1, 7, and 13-15 are in this application.

Reiection under 35 U.S.C 112

Claims 1 and 15 have been amended to recite "comprising" instead of "characterized by" as suggested by the Office.

Claims 2, 6, 7 and 16 have been cancelled so the rejection regarding the "derived" language and "fragments thereof" is moot.

The objected claims 3-5, 8-12 and 17-18 have been canceled.

Rejection under 35 U.S.C. 102

1. The Office rejected claim 1 under 35 U.S.C. 102 (b) as being anticipated by Ogasawara et al. (Lancet, Vo1.347,4/27/96, pages 1 183-1 184), hereinafter referred to as Ogasawara. This is respectfully traversed.

Anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference. *In re Paulsen*, 30 F.3d 1475, 31 USPQ 1671 (Fed. Cir. 1994). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991).

Ogasawara does not disclose that antinuclear antibodies are predictive of recurrent miscarriage. According to Ogasawara, antinuclear antibodies are somehow associated with miscarriage but the presence of
such antibodies does not predict recurrent miscarriage.

"We conclude that ANA are associated in some way with miscarriage, but ANA-positive recurrent aborters with no evidence of aPL do not require medication because the presence of antibodies does not predict subsequent pregnancy loss"
(See the last paragraph of Ogasawara).

Therefore, Ogasawara actually teaches away from the present invention.

Nevertheless, claim 1 has been amended. The amended claim 1 relates to a method of diagnosing immunological recurrent spontaneous abortion by determining the level of an antinuclear antibody against human chromosome No.2.

Ogasawara does not teach a diagnosis of immunological recurrent spontaneous abortion by measurement of antinuclear antibodies, let alone the measurement of the specific antinuclear antibodies against human chromosome No.2.

Therefore, as Ogasawara does not disclose each element of the claim it is respectfully requested that the rejection be withdrawn.

2. The Office rejected claim 15 under 35 U.S.C. 102 (b) as being anticipated by Kwak et al. (Journal of Reproductive Immunology, 1995, Vol.28, pages 175- 188), hereinafter referred to as Kwak. This is respectfully traversed.

Claim 15 has been amended. The amended claim 15 relates to monitoring a therapeutic effect for immunological spontaneous abortion by determining the level of an antinuclear antibody against human chromosome No.2.

Kwak does not teach or suggest measurement of an antinuclear antibody against human chromosome No.2.

Therefore, as each element of the claim is not disclosed in the reference, it is respectfully requested that the rejection be withdrawn.

Reiection under 35 U.S.C 103

1. The Office rejected claims 2-6 under 35 U.S.C. 103 (a) as being unpatentable over Ogasawara and in view of Bernasconi et al. (American Journal of Human Genetics, 1996, Vol.59, No.5 pages 11 14-1 118), hereinafter referred as Bernasconi. This is respectfully traversed.

As discussed in the above, Ogasawara failed to teach the claimed limitations of amended claim 1. Bernasconi does not overcome the basic deficiencies of Ogasawara.

The Office stated that Bernasconi teaches the evaluation of spontaneous abortion in a 36 year old normal healthy female. Cytogenic investigation disclosed a female karyotype with isochromosomes of 2p and 2q replacing two normal chromosomes 2. It appeared that chromosome No.2 was important in the patient's pregnancies.

Applicant respectfully requests reconsideration. A karyotype with isochromosomes of 2p and 2q does not teach or suggest determining antinuclear antibody against an isolated chromosome No. 2 as claimed in this application.

Bernasconi does not even suggest that there is a causal relationship between the abnormal karyotype and RSA. Bernasconi merely reported a single case wherein a woman with RSA had an abnormal karyotype. Nothing more. In fact, Bernasconi discloses that other chromosome such as 4-6, 8-11, 13, 20-22, and may be related to syndromes or spontaneous abortion. In the second column on page 1116, Bernasconi discloses that a newborn with maternal UPD2 with reduction of homozygosity at markers in the midportion of the long arm. This teaches that even with an abnormal UPD2, a pregnancy can be carried to term which is clearly a different result from spontaneous abortion.

The Office further stated that "[a]bsent evidence to the contrary the measurement of Chromosome No.2 is deemed obvious given the teaching of the prior art".

Applicant respectfully disagrees. According to MPEP 2141, citing *Hodosh v. Block Drug Co., Inc.,* 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n. 5 (Fed. Cir. 1986), when applying 35 USC 103, the following tenets of patent law must be adhered to:

1) the claimed invention must be considered as a whole;

2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; and

3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention.

The reason, suggestion or motivation to combine references may be found explicitly or implicitly. While the references need not expressly teach that the disclosure contained therein should be combined with another, the showing of combinability must be clear and particular. *Ruiz v. A.B. Chance Co.,* 57 USPQ2d 1161 (Fed. Cir. 2000).

According to the U.S. Supreme Court in KSR v Teleflex and as included in the Examination Guidelines for Determining Obviousness Under 35 USC 103 ""[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some

articulated reasoning with some rational underpinning to support the legal conclusion of obviousness."" This has not been shown.

Applicant notes that to establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. The Examiner has not met his burden as at least the foregoing elements of the claim are not taught or suggested by the prior art. There is no motivation or suggestion that measurements of the level of antinuclear antibody by using an isolated human chromosome No. 2 as an antigen can be used to diagnose immunological recurrrent spontaneous abortion.

Therefore, it is respectfully requested that this rejection be withdrawn.

2. The Office further rejected claims 7-12 and 16-18 under 35 U.S.C. 103 (a) as being unpatentable over Bernasconi, in view of Foster et al. (US. Patent #4,444,879), hereinafter referred as Foster. This is respectfully traversed.

Amended claim 7 relates to a kit for diagnosing immunological recurrent spontaneous abortion comprising an isolated human chromosome No.2 as antigen.
Bernasconi does not teach the use of isolated human chromosome No.2 for the diagnosis of immunological RSA. Bernasconi only reported a single case wherein a woman with RSA had a karyotype with isochromosomes of 2p and **2q.** Bernasconi did not teach any causal relationship between RSA and the abnormal karyotype. Even there were such causal relationship, one skilled in the art would examine the karyotype of chromosome No.2 of a potential patient, not use an isolated human chromosome No.2 as an antigen for determining the level of antinuclear antibody against chromosome No.2 as taught by the present invention. Therefore, Bernasconi does not disclose the limitations of the amended claim 7.

Foster only teaches the conventional components of a kit, not the key component in the present invention, i.e., an isolated human chromosome No.2 as antigen.

Therefore, the combination of Bernasconi and Foster does not render the amended

claim 7 obvious.

Therefore, it is respectfully requested that the rejection be withdrawn.

3. The Office also rejected claims 13-14 under 35 U.S.C. 103 (a) as being unpatentable over Bernasconi, in view of Foster, and further in view of further in view of Maggio (Immunoenzyme technique I, CRC press 1980, pages 186-187), hereinafter referred as Maggio. This is respectfully traversed.

As discussed above, amended claim 7 is not obvious over the combination of Bernasconi and Foster. As dependent claims from claim 7, claims 13 and 14 are also patentable over the same combination. Maggio does not have any teaching relating to diagnosis of immunological RSA or an isolated human chromosome No.2. Therefore, even Maggio is considered, claims 13 and 14 are unobvious.

Therefore, it is respectfully requested that this rejection be withdrawn.

Other Issues

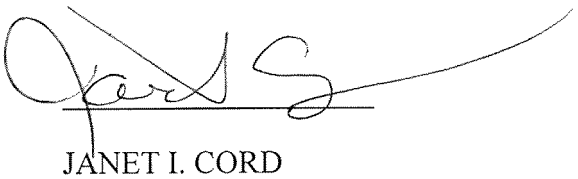
Page 1 of the specification has been amended to include reference to PCT/CN04/00134.

A new Abstract has been added.

The first page of the specification was numbered "1". A copy of this page from PAIR is attached.

It is submitted that the application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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